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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/647,596 01/16/01 VAN EMBDEN

J 41497

000466 HM12/0710
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EXAMINER

SQUAYA, J

ART UNIT	PAPER NUMBER
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1655

DATE MAILED:

07/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/647,596

Applicant(s)

Van Embden et al

Examiner

Jehanne Souaya

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 16, 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3 20) ☐ Other: _____

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DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Escherichia Coli in Paper No.8 is acknowledged. The traversal is on the ground(s) that the restriction requirement is improper and unsustainable as a matter of law in that it does not purport to associate any of claims 1-15 with any of the 15 identified groups. This is not found persuasive because claims 1-25 are considered linking claims in that all claims would be examined, but only to the extent that they are directed to a single patentably distinct bacteria and repeat sequence. Thus in the present case, claims 1-25 will be examined wherein the bacteria repeat sequence is that from E. Coli. This is not an election of species as the nucleic acid sequence of the repeat sequence for each bacteria are different and are patentably distinct (see Restriction Requirement in previous communication). The response states that the present application illustrates the applicability of the method in detecting other bacteria than E. Coli. This argument was not found persuasive as a patent to the method claims directed to a single bacterium would stand alone. That is, a patent to the general method would not be obvious over another bacterium if the sequence of the direct repeat region were unknown or if it were unknown in the prior art that such a bacterium possessed a direct repeat sequence. Furthermore, although E. Coli and Salmonella both belong to Enterobacteriaceae, they are patentably distinct organisms possessing different genomes.

The requirement is still deemed proper and is therefore made FINAL.

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Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Embden et al (WO 95/31560) and Accession numbers M27059 and M27060.

The claims are drawn to a method for the in vitro amplification of nucleic acids and the detection and differentiation of bacteria using primers that are sufficiently complementary to a part of the Direct Repeat sequence of E.coli, wherein the Direct Repeat is between 20-50 base pairs and occurs 5-60 times in the region of the bacterial genome and wherein the direct repeat sequences are separated by spacer sequences with a length between 20-50 nucleotides.

Van Embden et al teaches a method for the in vitro amplification of nucleic acids, the detection of M. tuberculosis, and the differentiation of M. tuberculosis from other bacteria, using amplification primers wherein a pair of primers is used comprising oligonucleotides sequences sufficiently complementary to a part of the direct sequence of a bacterium belonging to the M. tuberculosis complex of microorganisms (see abstract). Van Embden teaches that due to the multiple presence of direct Repeats in the microorganisms to be detected, the use of such primers implies that all the spacer regions will be amplified in an efficient manner (see p. 7). Van

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Embden teaches that in particular it is not necessary for extremely long sequences to be produced in order to obtain amplification of spacers located at a distance from the primer. Van Embden teaches that with the selection of the pairs a heterogeneous product is obtained comprising a lot of smaller fragments all comprising spacer region nucleic acid. Van Embden teaches that subsequently the detection of the amplified product can occur simply by using an oligonucleotide probe directed at one or one of the spacer regions one wishes to detect and that in order to avoid hindrance in the amplification reactions the primers can have oligonucleotide sequences complementary to non-overlapping parts of the direct repeat sequence so that when both primers hybridize to the same direct repeat and undergo elongation they will not be hindered by each other. Van Embden further teaches that in particular to avoid any hindrance during elongation reactions when one primer DRA is capable of elongation in the 5' direction and the primer DRB is capable of elongation in the 3' direction, the DRA is selected such that it is complementary to a sequence of the Direct Repeat located to the 5' side of the direct repeat to which DRB is complementary. Van Embden further teaches that a probe can be used to carry out the invention wherein the probe is capable of hybridizing to a spacer sequence and comprises at least 7 consecutive nucleotides homologous to the spacer sequence and/or exhibiting at least 60% homology with the spacer. Van Embden teaches primers, probes, and kits to carry out the method of the invention.

Although Van Embden does not teach such amplifying, detecting or differentiating E. Coli using primers to the direct repeat sequence of E. Coli, such a sequence was known and taught in

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the art at the time of the invention. Applicant's own specification discloses such knowledge and teaches Genbank Accession numbers M27059 and M27060 which teach the region of E.coli comprising the direct repeat sequences. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Van Embden for the purpose of detecting and differentiating E. Coli from other bacteria as Van Embden an efficient method of doing so for M. tuberculosis complex bacteria. The ordinary artisan would have been motivated to modify the method of Van Embden to detect E. Coli with the general method taught by Van Embden as the state of the art is very high with regard to detecting and differentiating E. Coli as well as other bacteria for purposes such as diagnosis of specific infection.

With regard to claim 2, which is drawn to the limitation of using the program Patscan to obtain the Direct Repeat sequence, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to automate screening for a direct repeat sequence from a bacteria for the purpose of optimizing and obtaining the best possible sequence for use in a method to differentiate and detect a specific bacteria from other bacteria. The state of the art at the time of the invention was very high with regard to determining sequences with similarities and differences between different bacteria for the purpose of differentiating and detecting specific types of bacteria. As the Patscan program was known and readily available at the time of the invention, the ordinary artisan would have been motivated to automate the screening of a bacterial

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genome to obtain the best possible sequence from the direct repeat region for the purpose of detecting and differentiating a specific bacteria. SEE MPEP 2144.04 which states:

III. AUTOMATING A MANUAL ACTIVITY

In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." **The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.**)

With regard to claim 7 which is drawn to the limitation that the direct repeat sequence is not prone to loop formation or any obvious secondary structure, it would have been prima facie obvious to one of ordinary skill in the art to target a sequence that was not prone to loop formation or any obvious secondary structure as it was well known in the art at the time the invention was made that such secondary structure could inhibit or undermine methods relying on specific hybridization of a probe or primer to a target sequence.

4. No claims are allowable.
5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

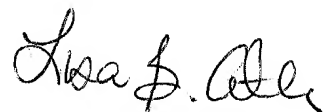
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.



LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800-1600



Jehanne Souaya
Patent examiner

June 15, 2001